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10/551,475	09/30/2005	Michael George	Q111431	4410
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SUGHRUE MION, PLLC 2100 PENNSYLVANIA AVENUE, N.W. SUITE 800 WASHINGTON, DC 20037			BOESEN, CHRISTIAN C	
			ART UNIT	PAPER NUMBER
			1639	
			NOTIFICATION DATE	DELIVERY MODE
			11/27/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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<b>Office Action Summary</b>	<b>Application No.</b> 10/551,475	<b>Applicant(s)</b> GEORGE ET AL.
	<b>Examiner</b> CHRISTIAN BOESEN	<b>Art Unit</b> 1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(o).

#### Status

- 1) Responsive to communication(s) filed on 12 August 2009.
- 2a) This action is FINAL.      2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 47-55,57,59,60,63-79,83,84,86-89 and 92-100 is/are pending in the application.
- 4a) Of the above claim(s) 48-55,57,59,60,63,67,69-79,83,84,86-89 and 92-100 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 47, 64-66, 68, and 91 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftperson's Patent Drawing Review (PTO 646)
- 3) Information Disclosure Statement(s) (PTO/SB/08)  
 Paper No(s)/Mail Date 08/12/2009
- 4) Interview Summary (PTO-413)  
 Paper No(s)/Mail Date \_\_\_\_\_
- 5) Notice of Informal Patent Application
- 6) Other: \_\_\_\_\_

**DETAILED ACTION**

This Final Office Action is responsive to the communication received 08/12/2009.

***Claim Status***

Claim(s) 99-100 have been added as filed on 08/12/2009.

Claim(s) 64, 66, 68 and 91-93 have been amended as filed on 08/12/2009.

Claim(s) 47-55, 57, 59-60, 63-79, 83-84, 86-89 and 92-100 are currently pending.

Claim(s) 48-55, 57, 59-60, 63, 67, 69-79, 83-84, 86-89 and 92-100 have been withdrawn.

Claim(s) 47, 64-66, 68, and 91 are being examined in this application.

***Election/Restrictions***

Applicant's election with traverse in the reply filed 02/20/2009 of group IV, claims 47, 64-68, 70 and 88-91 is noted. Applicant election in the reply filed 02/20/2009 of the species where the Lig corresponds to salmeterol and the Tag corresponds to BODIPY-630/650 is noted.

This application contains claim(s) 48-55, 57, 59-60, 63, 67, 69-79, 83-84, 86-89 and 92-100 drawn to an invention nonelected with traverse in the reply filed on 02/20/2009. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

***Priority***

This application for patent is filed under 35 U.S.C 371 of PCT/GB04/01418 (filed on 03/31/2004).

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Acknowledgment is made for priority to a provisional application 60/465,807 04/28/2003.

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in United Kingdom on 04/02/2003. The applicant has filed a certified copy of the 0307559.5 application as required by 35 U.S.C. 119(b).

#### ***Information Disclosure Statement***

The information disclosure statement (IDS) submitted on 08/12/2009 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the Examiner.

#### **Specification Objection(s) Withdrawn**

Upon further consideration and in light of Applicant's arguments and/or amendments, the following specification rejection(s) as set forth in the previous office action is(are) withdrawn:

1. The disclosure is objected to because of the following informalities. The use of trademarks (i.e. BODIPY™, Cascade Blue™, and Texas Red™) has been noted throughout this application (i.e. page 3, line 3).

#### **Claim Rejection(s) Withdrawn**

Upon further consideration and in light of Applicant's arguments and/or amendments, the following claim rejection(s) as set forth in the previous office action is(are) withdrawn:

1. Claims 64, 66, 68, and 91 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

**Claim Objection(s) / Rejection(s) Maintained**

*Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 47, 64-66, 68, and 91 are rejected under 35 U.S.C. 103(a) as being unpatentable over McCrea (Molecular Pharmacology 1996 volume 49 pages 927-937) in combination with (US Patent 6,171,794 B1).**

Claims are drawn to a fluorescently tagged nucleoside ligand for adenosine A1 and other G protein coupled receptors. The elected species is BODIPY-630/650 tagged salmeterol. The chemical structure of the elected ligand species corresponds to CAS Registry number 89365-50-4 that is identical to the compound named salmeterol with the CAS Registry number 89365-50-4.

McCrea teaches that salmeterol, which is a ligand for  $\beta_1$ - and  $\beta_2$ -adrenoceptors (see entire document). Cells containing stimulated  $\beta_1$ - and  $\beta_2$ -adrenoceptors accumulate cAMP (see page 928 and figure 1). The accumulation of cAMP is measured by stimulating C6 cell monolayers with salmeterol and measuring the conversion of radiolabeled adenine (8-[<sup>3</sup>H]Adenine) into [<sup>3</sup>H]cAMP (see table 1 and figures 1-5).

While McCrea teaches using a radiolabel to determine the duration of salmeterol action, McCrea does not expressly teach a fluorescently tagged salmeterol.

Burchard teaches labeling nucleotide analogues with the fluorescent label BODIPY-630/650 (see column 9 line 43 and claim 14).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to label McCrea's salmeterol with Burchard's fluorescent label BODIPY-630/650 to arrive at applicant's invention with the above cited references before them.

One would have been motivated to label McCrea's salmeterol with Burchard's fluorescent label BODIPY-630/650 because Burchard teaches that fluorescent labels are preferred to other types of labeling including radioactive isotopes (see column 9 lines 24-33).

One would have had a reasonable expectation of success to label McCrea's salmeterol with Burchard's fluorescent label BODIPY-630/650 because techniques for labeling nucleotide analogues are well established in the art as evidenced by Burchard (see column 9 lines 24-33).

Thus the present invention would have been *prima facie* obvious at the time the invention was made.

*Discussion and Answer to Argument*

Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

I. *Applicant asserts "Neither McCrea nor Burchard, alone or in combination, discloses or suggests monitoring GPCR ligand binding of any kind, nor any labeling of GPCR ligands, in living cells or in any other form." "McCrea fails to teach or suggest the location of the receptors in the cell at which salmeterol is binding. Therefore, one of ordinary skill in the art would not have been motivated to look to the BODIPY<sup>TM</sup> labeling because the focus of the study in McCrea was relating to the beta-adrenoceptors, namely their identity and susceptibility to agonists and antagonists, not for the purpose of measuring cAMP." (Reply page 90 center).*

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "*monitoring GPCR ligand binding*", "*labeling of GPCR ligand*", etc.) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the

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specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

It is also noted that the instant claims are drawn to products but not to methods.

Applicants also argue there is no motivation to combine the cited references. In response to Applicant's arguments, the Examiner respectfully disagrees. Applicant asserts "*Neither McCrea nor Burchard, alone or in combination, discloses or suggests monitoring GPCR ligand binding of any kind*". McCrea is indirectly measuring **salmeterol** binding to two different types of **GPCR receptors**, for example,

"Comparison of duration of **agonist action at  $\beta_1$ - and  $\beta_2$ -adrenoceptors** in C6 glioma cells: evidence that the long duration of action of salmeterol is specific to the  **$\beta_2$ -adrenoceptor**" (page 927 title).

McCrea is measuring the indirect binding of salmeterol, a GPCR ligand. The binding of the agonist ligand salmeterol to GPCR stimulates the disassociation of the G-protein complex allowing the free G<sub>s</sub> subunit to interact with adenylate cyclase to stimulate the production of cAMP that is measured in the form of [<sup>3</sup>H]-cAMP. Thus, the binding of the agonist ligand salmeterol to GPCR, incubation, and the measurement of [<sup>3</sup>H]-cAMP are linked through the free G<sub>s</sub> subunit and adenylate cyclase. The BODIPY labeled salmeterol in the present application can also be used to measure the binding of ligand salmeterol to GPCR. The Examiner agrees that direct labeling of salmeterol would allow for the determination of the location of receptors that bind the ligand salmeterol. Burchard teaches a BODIPY labeled nucleotide used in binding studies. The ability to measure receptors directly is a reason to substitute the Burchard's nucleotide with McCrea's nucleoside (salmeterol) to generate a BODIPY labeled salmeterol.

In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Further, Applicants are also respectfully directed to the Supreme Court decision, which forecloses the argument that a specific teaching, suggestion, or motivation is required in the references to support a finding of obviousness. *KSR, 127 S.Ct. at 1741, 82 USPQ2d at 1396.*

2. *Applicant asserts "Burchard is directed to distinguishing nucleic acid sequences by their hybridization properties with nucleic acid probes. Burchard discloses labeling the target polynucleotide sequence in a sample, applying an immobilized probe or probes to the sample under hybridization conditions, and washing off and removing any polynucleotide sequences which are not hybridized or bound to the probe or probes. The amount of labeled polynucleotide remaining can then be measured (see column 4, lines 1-5, lines 44-49;and column 9, lines 12-17). However, Burchard fails to disclose ligand binding for GPCR receptors. Rather, Burchard discloses BODIPY<sup>TM</sup> labeling of polynucleotide, not the particular challenges associated with attaching a fluorophore in such a way as to retain pharmacological activity in view of the fact that the ligand binding site for GPCR receptors is usually deep within the transmembrane regions of the receptor. Contrary to the Examiner's assertions, it would not have been prima facie obvious to employ a label such as BODIPY<sup>TM</sup> in "a GPCR ligand, inhibitor, or intracellular enzyme or a substrate or inhibitor of a drug transporter", as claimed by the Applicant." (Reply page 90 bottom).*

In response to Applicant's argument that the references fail to show certain features of Applicant's invention, it is noted that the features upon which Applicant relies (i.e., *attaching a fluorophore in such a way as to retain pharmacological activity*) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Further, Applicants are also respectfully directed to the Supreme Court decision, which forecloses the argument that a specific teaching, suggestion, or motivation is required in the references to support a finding of obviousness. *KSR, 127 S.Ct. at 1741, 82 USPQ2d at 1396*.

3. *Applicant asserts "the claimed invention is not a mere recitation of salmeterol plus BODIPY, rather, Applicant's claimed invention is related to a compound of formula I, such a formula being neither disclosed nor suggested anywhere in the cited prior art. Indeed, Applicant's disclosure emphasizes the importance of the design of the compound, the tag having a specific influence on the pharmacology of the resulting product (see page 5, lines 23-27 of the specification)." (Reply page 91 center).*

In response to Applicant's argument that the references fail to show certain features of Applicant's invention, it is noted that the features upon which Applicant relies (i.e., *the*

*importance of the design of the compound, the tag having a specific influence on the pharmacology of the resulting product) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).*

In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to Applicant's arguments, the Examiner respectfully disagrees. McCrea teaches a nucleoside (salmeterol) that corresponds to "Lig" in formula 1. Burchard teaches a covalently BODIPY labeled nucleotide. BODIPY corresponds to "J<sub>T</sub>Tag" in formula 1. The covalent bond between BODIPY and the labeled nucleotide corresponds to "L" in formula 1. Substituting Burchard's nucleotide with McCrea's nucleoside (salmeterol) to generate a BODIPY labeled salmeterol yields a compound that where salmeterol corresponds with "LigJ<sub>T</sub>" in formula 1.

4. *Applicant asserts "neither McCrea et al nor Burchard discloses or suggests the capability of carrying out its respective disclosed method in vivo. Burchard performs its method on samples of polynucleotides, to which immobilized probes are applied so that the unhybridized polynucleotides can subsequently be washed away. The assay used by McCrea relies on lysis of the cells and therefore it provides no teaching concerned with the use of monitoring salmeterol binding in living cells. There is no teaching in McCrea of visualizing the location of beta*

*adrenoceptors by culturing the cells in fluorescent media such as GFP (green fluorescent protein) together with fluorescent salmeterol, and imaging the green fluorescent cell surface (outlined by GFP fluorescence) and the contrasting red or blue fluorescent agonist bound to beta adrenoceptors. Nor is there teaching of introducing antagonists and determining the change in visualization of adrenoceptors." (Reply page 91 bottom).*

The instant claims are drawn to products, but not to methods. In response to Applicant's argument that the references fail to show certain features of Applicant's invention, it is noted that the features upon which Applicant relies (i.e., *the capability of carrying out its respective disclosed method in vivo*) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In response to Applicant's argument that *the capability of carrying out its respective disclosed method in vivo*, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

5. Applicant asserts "Applicants submit that neither McCrea nor Burchard teaches the concept of visualizing whole cells without lysis to determine information. In fact, McCrea teaches away from the present invention by concentrating on lysis of cells and investigating cell contents. Moreover, Burchard further teaches away by looking at nucleic acid molecules, and not at cells or cell contents." (Reply page 92 center).

In response to Applicant's arguments, the Examiner respectfully disagrees. Teaching away involves teaching that the Applicant's present invention would not be possible (i.e. it would not be possible to create a BODIPY labeled salmeterol). Burchard teaches measuring binding of labeled nucleic acids, this is not "teaching away" from the Applicant's present invention.

In response to Applicant's argument that the references fail to show certain features of Applicant's invention, it is noted that the features upon which Applicant relies (i.e., *the concept of visualizing whole cells without lysis to determine information*) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In response to Applicant's argument that *the concept of visualizing whole cells without lysis to determine information*, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

6. *Applicant asserts "as disclosed in Figures 1 and 2, Applicants have obtained unexpectedly accurate and detailed results, with very precise visualization of cell surface receptors, which show a precise overlay of cell surface and receptor sites. Applicants have shown that by incorporating a linker in the claimed fluorescently tagged (ant)agonists, the receptor binding is not affected or influenced by the presence of the bulky fluorescent*

*component. This result was not expected and has not previously been demonstrated."* (Reply page 92 bottom).

In response to Applicant's arguments, the Examiner respectfully disagrees. It is not unexpected that a fluorescent labeled nucleoside would maintain the ability to bind a receptor. Burchard teaches that a fluorescent labeled nucleotide maintains the ability to bind to complementary nucleotides. It is known to label ligands for visualization of receptors *in vivo*. Farinas (03/19/1999 The Journal of Biological Chemistry volume 274 page 7603) teaches a fluorescent labeled small molecule ligand can bind a protein receptor on cell membranes *in vivo*, for example, Figure 1, Figure 2, and

"**A cell labeling** method is reported here that combines the site specificity conferred by genetically encoded targeting sequences with the excellent spectral and indicator properties of small chemical **fluorophores**. The strategy is to express a high affinity "receptor" at a specified intracellular location to trap a conjugate of a **fluorophore linked to a receptor "ligand"**" (Fig. 1a). We chose a **single-chain antibody (sFv)** ... as the receptor and a hapten (phOx) as the **ligand**. Although many receptor-ligand pairs are possible, the antibody-hapten pair was selected because of the simple ligand-probe chemistry and high affinity interaction without interference from cellular factors. For sFv targeting, cells are transfected with cDNAs encoding sFv in fusion with targeting sequences. **Fluorophore-hapten conjugates** are added to the extracellular solution at low concentrations, diffuse to sites of sFv expression, and bind to the sFv. Conjugates of different indicator and spectral properties were synthesized (Fig. 1b), including phOx-Bodipy FL (green fluorescent), phOx-fluorescein (green fluorescent, pH-sensitive), and phOx-tetramethylrhodamine (red fluorescent). **The flexible linkers were designed to permit stacking of the unbound hapten with its covalently attached fluorophore to form a dark complex and reduce background fluorescence.** The ability to label cellular sites with fluorescent probes with varied spectral and indicator properties was demonstrated,..." (page 7603 right top).

phOx and salmeterol are both types of small molecule ligands. sFv and GPCR are both types of protein receptors.

In response to Applicant's argument that the references fail to show certain features of Applicant's invention, it is noted that the features upon which Applicant relies (i.e., *by*

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*incorporating a linker in the claimed fluorescently tagged (ant)agonists, the receptor binding is not affected or influenced by the presence of the bulky fluorescent component*) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

### Summary

McCrea teaches the indirect measurement of the unlabeled nucleoside ligand (salmeterol) with a GPCR by measuring [<sup>3</sup>H]-cAMP production. Burchard teaches the direct measurement of BODIPY labeled nucleotide binding. Burchard teaches that a fluorescent label (i.e. BODIPY) is preferred to a radiolabel (i.e. [<sup>3</sup>H]). In order to measure the binding of a nucleoside ligand (salmeterol) to a GPCR directly, one would be motivated to substitute McCrea's nucleoside (salmeterol) for Burchard's nucleotide to yield BODIPY labeled salmeterol.

Applicant's arguments related to pharmacological activity, *in vivo* binding studies and linker influenced receptor binding are not in the examined claims.

### *Double Patenting*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re*

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*Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

**Claims 47, 64-66, 68, and 91 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21-24 of copending Application No. 11/576,035.**

Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims are drawn to a fluorescently tagged nucleoside ligand for adenosine A1 and other G protein coupled receptors. The claims of the copending Application 11/576,035 are drawn to an assay using a fluorescently tagged nucleoside ligand for adenosine A1 and other G protein coupled receptors.

Therefore the present claims are obvious in view of the claims of the copending Application 11/576,035.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

*Discussion and Answer to Argument*

Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below:

Applicants requested the ODP rejection be held in abeyance. Applicants have not provided any specific traversal over the above ODP rejection. Thus, the above rejection is maintained for the reasons of record.

***Conclusion***

No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to CHRISTIAN BOESEN whose telephone number is 571-270-1321. The Examiner can normally be reached on Monday-Friday 9:00 AM to 5:00 PM.

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If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Christopher S. Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Christian Boesen/  
Examiner, Art Unit 1639

/SUE LIU/  
Primary Examiner, Art Unit 1639